REMARKS

In the present amendment, claims 38 and 40 have been amended, claim 39 has been cancelled and new claims 41-42 have been added. Support for the amendments can be found throughout the specification and claims as originally filed. For example, support for the amendment of claim 38 can be found, at least at page 4, lines 4-14, and in Figure 5. Support for new claims 41 and 42 can be found, for example, at least at page 6, lines 13-33, and at page 10, line 27 to page 11, line 5. *No new matter has been added.*

Accordingly, upon entry of the present amendment, claims 16-2, 38 and 40-42 will be pending. Any amendments to and/or cancellation of the claims should in no way be construed as acquiescence to any of the rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed or as previously pending in this or a separate application(s).

Telephonic Interview

Applicants gratefully thank the Examiner for the courtesy of the telephonic interview held on May 17, 2005 with the undersigned, during which the outstanding rejections of record were discussed. In particular, as noted on the Interview Summary dated May 23, 2005, draft claim amendments were discussed with respect to the rejections under 35 U.S.C. §112, and the art cited under 35 U.S.C. §102 was also discussed. Accordingly, a detailed description of the support for the claims as amended is included herein.

Withdrawal of Rejections

Applicants gratefully acknowledge the withdrawal the rejections set forth in the previous Office Action, and the allowance of claims 16-21.

Claim Rejections – 35 USC §112, second paragraph

Claims 38 and 39 were rejected as being indefinite on the ground that "The term 'high stringency' is a relative term whose metes and bounds are not clear because one

skilled in the art use specific ionic and temperature conditions for hybridization." (Office Action at page 3, second paragraph).

Applicants respectfully submit that this rejection does not apply to claim 38 because the language of the claim *does not* include the phrase "high stringency." With respect to claim 39, Applicants maintain that high stringency conditions are standard in the art and well within the skill of the ordinary artisan. Moreover, specific conditions are disclosed in the Applicants' priority document at page 2, lines 22-28. However, solely in the interest of expediting prosecution, claim 39 has now been cancelled, and claim 40 has been amended to remove its dependency on the cancelled claim. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claim Rejections – 35 USC §112, first paragraph

Claims 38-40 were rejected on the ground that the subgeneric limitations set forth in these claims are not disclosed in the specification. Specifically, the terms "amiloride-sensitive," and "hybridizes at high stringency," were objected to as being new matter.

Applicants respectfully traverse this rejection. As stated in the Amendment filed on August 9, 2004, support for the term "amiloride-sensitive" may be found in the specification at least at page 4, lines 1-17. Additional support may also be found, for example, at page 3, lines 27-29, in Figure 5, and in the description of Figure 5 at page 7, line 36 to page 8, line 3. Further, in accordance with the discussion between the Examiner and the undersigned, claim 38 has now been amended to state that the slow component is "inhibited by amiloride," to more specifically set forth the subject matter which Applicants view as the invention. Reconsideration and withdrawal of this rejection is therefore requested.

With respect to the phrase "hybridizes at high stringency," Applicants reiterate that support for this phrase may be found in the specification, for example, at page 8, lines 4-9; at page 10, lines 19 to 25, and in the priority document. However, solely to expedite prosecution, claim 39 has been cancelled and claim 40 amended, thus rendering this rejection moot.

Claim Rejections under 35 U.S.C. §102

Claims 38-40 were rejected under 35 U.S.C. §102(b) as being anticipated by Waldman *et al.* (J. Biol. Chem., 1997) on the ground that this reference discloses a proton gated sodium channel which has 85.6% amino acid sequence identity with SEQ ID NO:2, and which are amiloride sensitive.

Applicants respectfully traverse this rejection. The presently claimed subject matter is drawn to a *"**human** proton-gated cation channel comprising a subunit that comprises an amino acid sequence that is **at least 85% identical** to the amino acid sequence of SEQ ID NO: 2, wherein the proton-gated cation channel displays a biphasic current when activated by an extracellular proton concentration which is below physiological pH, and wherein **the slow component of the biphasic current is inhibited by amiloride**."*

In contrast, Waldman *et al.* disclose the ***rat*** DRASIC cation channel that is approximately ***83% identical*** to the amino acid sequence of SEQ ID NO: 2, wherein the ***slow component biphasic current is potentiated by amiloride.*** With respect to the assertion set forth in the Office Action that the amino acid sequence disclosed by Waldman *et al.* is 85.6% "identical" to the amino acid sequence of SEQ ID NO:2, Applicants respectfully point out that this position appears to be based on an misinterpretation of the sequence comparison provided by the USPTO. This sequence comparison appears to indicate that there is an 85.8% *similarity* between the two sequences, but specifically indicates that 445 out of 533 amino acids are exact, *i.e.*, identical matches. By doing a straightforward calculation: 445/533 = .8349, it is clear that the two full-length sequences are actually 83.5% identical (see also, Appendix A "Pairwise Alignment").

In view of the above, Applicants respectfully submit that the teachings of Waldman *et al.* do not anticipate the present claims and reconsideration and withdrawal of this rejection is requested.

Claims 38-40 were rejected under 35 U.S.C. §102(e) as being anticipated by DeWeille *et al.* (U.S. 6,287,859) on the ground that SEQ ID NO:14 discloses the amino

acid sequence of a proton gated cation channel that is 99.4% identical to the amino acid sequence of SEQ ID NO:2 of the present application.

Applicants respectfully submit that this rejection is improper. Functional homopolymeric and heteropolymeric (e.g., with P2X2) cation channels containing polypeptides having the amino acid sequence of SEQ ID NO: 2; channels containing polypeptides consisting essentially of this sequence; and channels containing polypeptides encoded by nucleic molecules that hybridize to the disclosed cDNA sequence under specific hybridization conditions, and variations thereof were provided in Applicants priority document filed on October 29, 1997. Applicants' priority document thus demonstrates that Applicants were in position of the presently claimed subject matter prior to the earliest priority date of February 11, 1998, claimed by DeWeille *et al.* Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claims 38-40 were further rejected under 35 U.S.C. §102(b) as being anticipated by Lewis *et al.* (Nature 1995) on the ground that this reference discloses P2X2 cation channels that are heteromultimeric, and thus may inherently contain the subunit containing the amino acid sequence of SEQ ID NO:2 as claimed by Applicants.

Applicants respectfully traverse this rejection. Lewis *et al.* disclose a novel heteropolymeric P2X channel that contains ***rat*** P2X2 and ***rat*** P2X3 subunits. They also reported that coexpression of cDNAs encoding ***rat*** P2X2 and ***rat*** P2X3, *but not other combinations*, yielded ATP-activated currents that closely resembled those of sensory neurons. Lewis *et al.* do not teach ***human*** heteropolymeric channels of any kind as presently claimed. Moreover, there is no indication whatsoever in this reference that the HEK293 cells used by Lewis *et al.* contain *any* endogenous cation channel subunits remotely resembling SEQ ID NO: 2, let alone a sufficient quantity of this subunit to inherently allow the formation of functional heteropolymeric cation channels.

In view of the above, Applicants respectfully submit that the teachings of Lewis *et al.* do not anticipate the present claims, and reconsideration and withdrawal of the rejection is requested.

Claims 38-40 were also rejected under 35 U.S.C. §102(e) as being anticipated by Renard *et al.* (US 2002/0172000) on the ground that this published application discloses a proton gated ion channel (SEQ ID NO:6) which is 94.9% identical to SEQ ID NO:2.

Applicants respectfully traverse this rejection. Renard *et al.* claims priority to a 371(c) application, USSN 09/424,666, filed November 29, 1999, which was abandoned. The earliest priority claimed by Renard *et al.* is to EP97401196.7, filed on May 30, 1997 and published as EP0884386A1on December 16, 1998. This EP application *does not* disclose SEQ ID NO: 6. The first disclosure of SEQ ID NO: 6 occurred in PCT/EP98/02884 which claims priority to the EP application. This PCT application was filed May 15, 1998 and published as WO 98/54316 on December 3, 1998, after the priority claim of the present application.

Accordingly, Applicants respectfully submit that Renard *et al.* does not qualify as prior art under 35 U.S.C. §102(e), and withdrawal of this rejection is requested.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 12-0080 under Order No. PCI-017USRCE from which the undersigned is authorized to draw.

Dated: May 31, 2005

Respectfully submitted,

By _____

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